REMARKS

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the claims.

Status of the Claims

In the present Reply, claims 8 and 9 have been canceled without prejudice or disclaimer of the subject matter contained therein. Also, claims 1, 2, 6 and 7 have been amended. Finally, claim 10 has been added. Thus, claims 1-7 and 10 are pending in the present application.

No new matter has been added by way of these amendments and new claim because each amendment and new claim is supported by the present specification. For example, the amendment to claim 1 is found in the present specification at page 11, lines 8-25 and page 14, lines 10-19. Support for new claim 10 is found at the same areas of the present specification, as well as in originally filed claim 1. The amendments to claims 2, 6 and 7 are minor in character and are to merely conform to the preamble of claim 1. Thus, no new matter has been added.

Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Election/Restriction

As stated in paragraph 5 of the Office Action, a restriction has been made as follows:

Group I, claims 1-7, as drawn to a method of determining the activity of a cell cycle regulatory factor; and

Group II, claims 8-9, drawn to a method of diagnosing cancer.

Further, Applicants are required to elect a species as stated in paragraph 4 of the Office Action.

Applicants herein reaffirm their election of Group I, claims 1-7, and the species of CDK1.

Issues under 35 U.S.C. § 112, Second Paragraph

Claims 1-6 stand rejected under 35 U.S.C. § 112, second paragraph, for reasons of indefiniteness (see paragraphs 6-7 of the Office Action). Applicants respectfully traverse.

With regard to paragraph 6 of the Office Action, Applicants respectfully refer the Examiner to the scope of pending claim 1 as presented herein. A positive step is recited that relates back to the preamble.

With regard to paragraph 7 of the Office Action, Applicants respectfully submit that instantly pending claim 1 recites the removal of the excess label. Accordingly, claim 1 is clear and definite to one of skill in the art.

Thus, reconsideration and withdrawal of this rejection are respectfully requested.

Issues under 35 U.S.C. § 112, First Paragraph

Claims 1-6 stand rejected under 35 U.S.C. § 112, first paragraph, for asserted lack of enablement (see paragraphs 8 and 9 for the two rejections). Applicants respectfully traverse, and reconsideration and withdrawal of these rejections are respectfully requested.

With respect to paragraph 8, the Examiner states that the disputed claims (as previously presented) do not enable a method for determining the activity of a cell cycle regulatory factor. However, Applicants respectfully submit that instantly pending claim 1 is now directed to calculating the activity of a cyclin-dependent kinase. Thus, this rejection is rendered moot and/or has been overcome. Withdrawal of the rejection as stated in paragraph 8 of the Office Action is respectfully requested.

Similarly, with respect to paragraph 9 of the Office Action, Applicants respectfully submit that instantly pending claim 1 is now directed to calculating the activity of a cyclin-dependent kinase. Thus, this rejection (relating to a method of determining the activity of a cell cycle regulatory factor) is rendered moot and/or has been overcome. Withdrawal of the rejection as stated in paragraph 9 of the Office Action is respectfully requested.

Issues under 35 U.S.C. § 103(a)

Claims 1, 2, 3 and 6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan et al. (*J. Biol. Chem.*, Vol. 268, pp. 20443-20451 (1993); hereinafter referred to as "Pan") in view of S. Jeong and Nikiforv (*BioTecniques,* Vol. 27, pp. 1232-1238 (1999); hereinafter "Jeong") and K.C. Facemyer and Cremo (*Bioconjugate Chem.*, Vol. 3, pp. 408-413 (1992); hereinafter "Facemyer") (see paragraph 10 of the Office Action).

Also, claims 1 and 4 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan, Jeong and Facemyer, and in further view of Hemmila (*Clin. Chem.*, Vol. 33, pp. 359-370 (1985); hereinafter "Hemmila") (see paragraph 11 of the Office Action).

Finally, claims 1 and 5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan, Jeong and Facemyer, in further view of Strachan and Read (*Human Molecular Genetics*, section 20.2.5 (1999); hereinafter "Strachan") (see paragraph 12 of the Office Action).

Applicants respectfully traverse all rejections, and reconsideration and withdrawal of these rejections are respectfully requested. Applicants do not concede that a *prima facie* case of obviousness has been established with respect to all rejections.

Distinctions over the combination of Pan, Jeon and Facemyer (claims 1, 2, 3 and 6)

First, Applicants respectfully refer the Examiner to the scope of claim 1 as presented herein. The present invention is directed to a method of calculating the activity of cyclin-dependent kinase, including using an anti-cyclin dependent kinase antibody to catch the cyclin-dependent kinase and labeling the substrate by coupling a fluorophore or an enzyme with a sulfur atom of the introduced monothiophosphate group.

Second, Applicants respectfully submit that a *prima facie* case of obviousness has not been established. In particular, the requisite disclosure of all claimed features, the required level of motivation, and the required reasonable expectation of success are lacking as follows.

The cited primary reference of Pan describes a method for measuring activities of CDK2 and CDC 2 purified from HeLa cells. However, Pan fails to disclose or recognize catching CDK in a sample by an anti-CDK antibody, reacting ATP-γS with a substrate, labeling the substrate

with a fluorophore or enzyme, as well as measuring the fluorescence or enzyme from a labeled substrate. Thus, Pan fails to describe multiple features of the present invention. Also, the cited secondary references do not account for the deficiencies of the primary Pan reference.

In particular, the cited Jeong reference fails to describe catching CDK in the sample via an anti-CDK antibody, as well as failing to disclose removal of the excess fluorophore or enzyme (that do not label the substrate) from the labeled substrate.

Similarly, the cited Facemyer reference fails to disclose catching CDK in the sample via an anti-CDK antibody and removing the fluorophore or enzyme (that do not label the substrate) from the labeled substrate. Thus, a *prima facie* case of obviousness has not been established with respect to the rejection stated in paragraph 10 of the Office Action.

This is because U.S. case law squarely holds that a proper obviousness inquiry requires consideration of three factors: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) whether or not the prior art would have taught, motivated, or suggested to those of ordinary skill in the art that they should make the claimed invention (or practice the invention in case of a claimed method or process); and (3) whether the prior art establishes that in making the claimed invention (or practicing the invention in case of a claimed method or process), there would have been a reasonable expectation of success. *See In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *see also In re Kotzab*, 55 U.S.P.Q.2d 1313, 1316-17 (Fed. Cir. 2000); *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Here, not even the initial requirement of disclosure of all claimed features (e.g., catching CDK in the sample via an anti-CDK antibody; removal of the non-labeled fluorophore or enzyme) has been satisfied. Thus, the rejection in view of Pan, Jeong and Facemyer has been overcome.

Withdrawal of the rejection as stated in paragraph 10 of the Office Action is respectfully requested.

Applicants also submit that the requisite disclosure of all claimed features is lacking for another reason. The cited secondary reference of Facemyer discloses a method for measuring the activity of myosin light chain kinase after isolation and purification of the same. In the second paragraph of the left column of page 408, the Facemyer reference describes kinases which are known to use ATP-γS as a substrate, which includes phosphorylase kinase, cAMP dependent protein kinase, nuclear protein kinase II, cGMP dependent protein kinase, protein kinase C, kinase F_A, heme-regulated protein kinase, myosin light chain kinase, calmodulin-dependnet protein kinase II, and EGF-receptor-associated protein kinase. Thus, the cited Facemyer reference is silent regarding cyclin-dependent kinase as used in the present invention. Therefore, Facemyer again does not account for the deficiencies of the primary reference of Pan, and there is no disclosure of all claimed features even when the three references are combined. Withdrawal of this rejection under § 103(a) is respectfully requested.

Further, one of ordinary skill in the art would not have the requisite motivation to combine the disclosure of Pan and Jeong with that of Facemyer in order to achieve the present invention. As discussed above, Facemyer does not even recognize the nature of the problem to be solved, nor does the Facemyer reference describe cyclin-dependent kinase as instantly claimed. *In re Rouffet,* 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). Thus, the requisite motivation is lacking in that the skilled artisan would not combine Pan with Jeong and Facemyer since the present invention would still not be achieved.

In addition, one of ordinary skill in the art would not have the requisite reasonable expectation of success to combine the disclosure of Pan and Jeong with that of Facemyer in order to achieve the present invention. Applicants note that: "Obviousness requires one of ordinary skill in the art have a reasonable expectation of success as to the invention—'obvious to try' and 'absolute predictability' are incorrect standards." *Velander v. Garner*, 68, USPQ2d 1769, 1784 (Fed. Cir. 2003) (citing *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673 (Fed. Cir. 1988)). Here, since Facemyer lacks disclosure of, e.g., cyclin-dependent kinase, any use of the disclosure in this reference with Pan and Jeong amounts to an improper "obvious to try" rationale. Thus, Applicants submit that the requisite reasonable expectation of success is lacking and that a *prima facie* case of obviousness has not been established.

Overall, Applicants respectfully submit that the rejection as stated in paragraph 10 of the Office Action has been overcome. This is because the cited references, even when (improperly) combined, do not disclose all instantly claimed features. Further, the requisite motivation and reasonable expectation of success are lacking for the reasons stated above, and one of ordinary skill in the art could not even accomplish or produce what is instantly claimed (see pending claim 1). Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Distinctions over the Combination of Pan, Jeong, Facemyer and Hemmila (claims 1 and 4)

The deficiencies and improper combination of Pan, Jeong and Facemyer are discussed above. Adding the disclosure of the secondary reference of Hemmila does not make this

rejection any more proper, and Applicants submit that a *prima facie* case of obviousness has not been established (with respect to paragraph 11 of the Office Action).

The cited Hemmila reference discloses fluoroimmunoassays using FITC as a fluorescent label for substrates. However, just like the other three cited references, Hemmila fails to disclose catching CDK in the sample by using an anti-CDK antibody, reacting ATP-γS with a substrate in the presence of CDK, and calculating the activity of CDK as instantly claimed (see pending claim 1). Thus, a *prima facie* case of obviousness has not been established since the cited combination of Pan, Jeong, Facemyer and Hemmila still does not satisfy the requirement of disclosure of all claimed features. *In re Vaeck.* Further, adding Hemmila still does not mean the requisite level of motivation and reasonable expectation of success are met, as discussed above. The combination with Hemmila does not make the instant rejection as proper. Thus, Applicants respectfully submit that this rejection has been overcome and request withdrawal thereof.

Distinctions over the Combination of Pan, Jeong, Facemyer and Strachan (claims 1 and 5)

This rejection has been overcome for the same reasons discussed above (with respect to paragraph 10 of the Office Action). Strachan discloses an expression mapping. Although this secondary reference describes the use of a peroxidase as a protein label, this reference still fails to disclose a method of calculating the activity of CDK as instantly claimed. Thus, a *prima facie* case of obviousness has not been established since the cited combination of Pan, Jeong, Facemyer and Strachan still does not satisfy the requirement of disclosure of all claimed features. *In re Vaeck.* Further, adding Strachan still does not mean the requisite level of motivation and reasonable expectation of success are met, as discussed above (regarding the rejection stated in

paragraph 10 of the Office Action). Thus, Applicants respectfully submit that this rejection (as stated in paragraph 11) has been overcome and request withdrawal thereof.

Conclusion

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez (Reg. No. 48,501) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Dated: August 31, 2005

Respectfully submitted,

By _____

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